REMARKS

Upon entry of this amendment, claims 1-9, 17-20 and 24 are pending in the instant application. Claim 17 has been allowed. Claims 1, 2 and 19 have been amended herein without prejudice or disclaimer. Support for the claim amendments presented herein is found throughout the specification and in the claims as originally filed. For example, support for the *H. pylori* nucleic acid of at least 175 base pairs, as recited by amended claims 1 and 2, is found at least at page 2, lines 16-17; and at page 6, line 19 of the specification. Support for the method of detecting a human nucleic acid of at least 175 base pairs in a patient sample containing shed cells or cellular debris, as recited by amended claim 18, is found at least at page 2, lines 16-17; and at page 6, line 19 of the specification. Support for the method of detecting a human nucleic acid of at least 200 base pairs in a patient sample containing shed cells or cellular debris, as recited by amended claim 19, is found at least at page 4, lines 21-22 and at page 6, lines 19-24. Accordingly, no new matter has been added by these amendments.

Claim Rejections Under 35 U.S.C. §102(b)

Claims 1-6, 8 and 18:

The Examiner has maintained the rejection of claims 1-6, 8 and 18 under 35 U.S.C. §102(b) as being anticipated by Gramley *et al.*, J. Clin. Microbiol., vol. 37(7): 2236-40 (1999) ("Gramley"). With regard to claims 1, 6, 8 and 18, the Examiner has maintained that Gramley describes a method of detecting a *H. pylori* infection by detecting a *H. pylori* nucleic acid in a patient sample and identifying indicia of a *H. pylori* infection if the amount and length of the nucleic acid in the sample exceeds an amount indicative of an absence of *H. pylori* infection. With regard to claims 2-5, the Examiner has again asserted that Gramley describes a method of detecting high-integrity *H. pylori* in a patient sample and comparing the level of high-integrity *H. pylori* nucleic acid to a level of non- *H. pylori* nucleic acid in the sample.

Applicant notes that independent claims 1 and 2 have been amended herein to recite methods of detecting *H. pylori* nucleic acids, including high-integrity *H. pylori* nucleic acids, having a length of at least 175 base pairs. In addition, claim 18, as

amended herein, is directed to a method of detecting a human nucleic acid of at least 175 base pairs in a patient sample containing shed cells or cellular debris.

Thus, the pending claims, as amended herein, are directed to methods of detecting nucleic acids in a patient sample, wherein the nucleic acids have a length of at least 175 base pairs.

In contrast, Gramley does not describe methods of detecting a nucleic acid that is at least 175 base pairs long. As acknowledged by the Examiner at page 5 of the Office Action, Gramley describes the detection of a *H. pylori* nucleic acid having only 139 base pairs and the detection of a human nucleic acid having only 148 base pairs. (*See e.g.*, Gramley, p. 2238, col. 2, ¶2 and Figure 3). Thus, Gramley fails to teach every element of the methods recited by amended independent claims 1, 2 and 18 and their respective dependent claims (including claims 2-5 and 8). As such, these claims are novel over Gramley, and this rejection should be withdrawn.

Powell:

The Examiner has maintained the rejection of claims 1-6, 8, 18 and 20 under 35 U.S.C. §102(b) as being anticipated by International Patent Application WO 00/29618 by Powell *et al.* ("Powell"). With regard to claims 1, 6, 8 and 18, the Examiner has maintained that Powell describes a method of detecting a *H. pylori* infection by detecting a *H. pylori* nucleic acid in a patient sample and identifying indicia of a *H. pylori* infection if the amount and length of the nucleic acid in the sample exceeds an amount indicative of an absence of *H. pylori* infection. With regard to claims 2-5, the Examiner has again asserted that Powell describes a method of detecting high-integrity *H. pylori* in a patient sample and comparing the level of high-integrity *H. pylori* nucleic acid to a level of non-*H. pylori* nucleic acid in the sample. With regard to claim 20, the Examiner has asserted that Powell also discloses a method of determining the threshold of *H. pylori* infection based on the amount of *H. pylori* DNA present in a sample.

As described above, independent claims 1, 2 and 18 (and their respective dependent claims including claims 2-5, 8 and 20) have been amended herein to recite methods of detecting a nucleic acid in various patient samples, wherein the nucleic acid (*e.g.*, *H. pylori* nucleic acids (including high-integrity *H. pylori* nucleic acids) and human nucleic acids) has a length of at least 175 base pairs.

In contrast, Powell does not teach a method of detecting a nucleic acid that is at least 175 base pairs long. As acknowledged by the Examiner at page 5 of the Office Action, the Powell methods, like the Gramley methods, detected a *H. pylori* nucleic acid having only 138 base pairs and the detection of a human nucleic acid having only 148 base pairs. (*See e.g.*, Powell at page 12, lines 14-17 and at page 16, lines 6-7). Thus, Powell does not disclose every element of the claimed methods. As such, amended claims 1-6, 8, 18 and 20 are novel over the Powell reference, and this rejection should be withdrawn.

Claim Rejections under 35 U.S.C. § 103(a)

The Examiner has maintained the rejection of claims 7, 9, 19 and 24 under 35 U.S.C. §103(a) as being obvious over Gramley in view of U.S. Patent No. 6,143,529 to Lapidus *et al.* ("Lapidus"). The Examiner has asserted that while Gramley did not teach the addition of an ion chelator to the patient sample and immobilized probe hybridization assay, Lapidus describes methods of improving sensitivity and specificity of obtaining nucleic acids greater than 200 base pairs from patient samples using EDTA. According to the Examiner, it would have been obvious to combine the methods of Gramley and Lapidus to produce the claimed methods of detecting a nucleic acid in a patient sample.

Applicant contends that the Examiner has failed to establish a *prima facie* case of obviousness. A *prima facie* case of obviousness requires some suggestion or motivation, either in the references themselves or in the knowledge generally available in the art, to modify the reference or to combine reference teachings. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See also MPEP 706.02(j).

As noted above, the pending claims have been amended to recite methods of detecting a nucleic acid in various patient samples, wherein the nucleic acid (*e.g.*, *H. pylori* nucleic acids (including high-integrity *H. pylori* nucleic acids) and human nucleic acids) has a length of at least 175 base pairs. The instant specification describes, *e.g.*, at page 2, lines 2-14, that the detection of these longer nucleic acids is an indicia of an active *H. pylori* infection.

Again, Gramley does not describe the detection of a nucleic acid (*e.g.*, a *H. pylori* nucleic acid or a human nucleic acid) that is at least 175 base pairs long. As acknowledged by the Examiner, the Gramley methods detected an *H. pylori* nucleic acid that was only 139 base pairs long and a human nucleic acid that was only 148 base pairs long, and the only method of detecting a *H. pylori* infection require the detection of the presence or absence of these 139 and 148 base pair nucleic acids. Moreover, the Gramley reference does not describe or suggest using PCR primers to detect nucleic acids of any other length. Thus, there is no teaching or suggestion in this reference that would motivate one of ordinary skill in the art to modify the Gramley methods in order to detect nucleic acids longer than those described by Gramley.

Accordingly, the skilled artisan would have no motivation to combine the methods of Gramley with the Lapidus methods. The fact that references can be combined or modified does not render the resulting combination obvious unless the prior art also suggests the desirability of the combination. (*See* MPEP §2143.01, citing *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990)). As described above, there is no suggestion in the Gramley reference that would motivate a skilled artisan to modify the detection methods to detect nucleic acids that are at least 175 base pairs long. Thus, the mere fact that the Gramley and Lapidus references can be combined is not sufficient to establish a *prima facie* case of obviousness.

Moreover, an assertion that modifying the Gramley reference would have been within the ordinary skill of the art at the time the claimed invention was made because the cited references were individually known in the art at the time the instant application was filed is also insufficient to establish a *prima facie* case of obviousness without some objective reason to combine the references. (*See* MPEP §2143.01, citing *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pate. App. & Inter. 1993)). Thus, the mere fact that the Gramley and Lapidus references were known in the art individually at the time the instant application was filed does not render the claimed invention obvious, as there is no teaching or suggestion in the Gramley reference that would motivate one of ordinary skill in the art to modify the methods described therein.

Accordingly, Applicant believes that the Examiner has failed to establish a *prima facie* case of obviousness, and this rejection should be withdrawn.

CONCLUSION

On the basis of the foregoing amendments and arguments, Applicant submits that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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